

Citation:

Chardigny JM, Destailats F, Malpuech-Brugère C, Moulin J, Bauman DE, Lock AL, Barbano DM, Mensink RP, Bezelgues JB, Chaumont P, Combe N, Cristiani I, Joffre F, German JB, Dionisi F, Boirie Y, Sébédio JL. Do Trans fatty acids from industrially produced sources and from natural sources have the same effect on cardiovascular disease risk factors in healthy subjects? Results of the Trans Fatty Acids Collaboration (TRANSFACT) study *Am J Clin Nutr*. 2008 Mar; 87 (3): 558-566.

PubMed ID: [18326592](#)

Study Design:

Randomized, double-blind, controlled, cross-over trial

Class:

A - [Click here](#) for explanation of classification scheme.

Research Design and Implementation Rating:

POSITIVE: See Research Design and Implementation Criteria Checklist below.

Research Purpose:

To compare the effects of trans-fatty acids (TFA) from industrially produced and natural sources on HDL and LDL-cholesterol, lipoprotein particle size and distribution, apolipoproteins and other lipids in healthy adult subjects.

Inclusion Criteria:

- Normolipidemic
- Either male or female
- If male, of a waist size less than 102cm; and if female, of a waist size less than 88cm
- Complete medical questionnaire and examination.

Exclusion Criteria:

- Overweight patients
- Patients with symptoms of any acute or chronic illness
- Patients who do not complete the study.

Description of Study Protocol:**Recruitment**

- The trial was approved by the French authorities (CCPRB Auvergne, agreement no AU599)
- Subjects were asked for signed informed consent to take part in the trial
- Recruitment method used was not described.

Design

- The study is monocentric and has a randomized, double-blind, controlled, cross-over design
- The total duration of the intervention is eight weeks
- A one-week run-in period is used in order allow subjects to adapt their dietary habits to the study requirements
- A short wash-out period is used in order to prevent carry-over effect of the treatments and to minimize excessive drop-out.

Dietary Intake/Dietary Assessment Methodology

- Both experimental fats (industrial and natural) contained about 20–22% of monounsaturated TFA and the volunteers' daily experimental fat intake (54g), will represent about 11-12g per day of TFA or 5.4% of the daily energy (based on 2,000kcal per day). All the calculations for diet composition assumed that 37% of the daily energy is provided by lipids, which is slightly higher than recommended by French nutritional guidelines
- During the run-in period, subjects received regular food items. During the experimental periods, subjects consumed the foods with TFA from the two different sources; daily intake of these three foods was 20g of butter (80% fat content), 100g of cheese (31% fat content) and 22g of cookies (31% fat content). The lipids from the experimental products represented a $67.3 \pm 8.8\%$ of the daily energy intake provided by fat
- A dietitian provided instructions to the volunteers to avoid consumption of additional food items containing trans fatty acids during both three-week experimental periods. Subjects recorded their food consumption (study products and other items) three times during the study period, at week zero (run-in period) and at weeks three and seven (the last week of the two intervention periods). Dietary records were analyzed by a dietitian using MICRO 6 diet analyzer software (version 6.0; GENI, Villers-Les-Nancy, France) and the daily energy intake and the proportion of energy intake from different nutrient sources were calculated
- The experimental fats were deficient of essential fatty acids (linoleic and α -linolenic acids). Two sources of vegetable oils balanced in linoleic and α -linolenic acids were provided to the subjects (one liter of each oil for each subject each month). These oils were suitable for cooking or for use in salad dressings and their consumption was monitored by the dietitian.

Blinding Used

This is a double-blind trial, investigators and participants were blinded of the treatments.

Intervention

Diet with industry sources of trans-fatty acids vs. diet with natural sources of trans-fatty acids.
Cross-over participants after three weeks.

Statistical Analysis

- The number of subjects enrolled in the study was based on detection of a difference of 2.11 mg/dL in HDL-cholesterol, with a planned within-subject variability of 4.5mg/dL, a significance level of 5% (two-sided) and a power setting of 80%
- Results are presented on the per-protocol data set
- Plasma variables from the last week of each intervention period were analyzed by using a mixed model, with treatment as the fixed effect, subject as the random effect and sex as the covariate
- A secondary analysis was performed to examine the sex treatment interaction
- Given that conclusions about effects were the same for both models, only the results of the model with interaction are presented; effects were declared significant at $P < 0.05$
- Statistical analyses were performed with SAS software (version 8.2; SAS Institute Inc.)

Data Collection Summary:

Timing of Measurements

- Zero to one week equal to acclimating period, run-in period
- One to three weeks equal to either control or treatment group
- Three to four weeks equals washout period
- Four to seven weeks equals crossover, either control or treatment group.

Blood pressure, fasting body weight and fasting blood sample for HDL-C, LDL-C, total cholesterol, lipoprotein levels and sub-classes and other parameters were measured at week zero, end of week two, end of week three, end of week four, end of week six and end of week seven.

Dependent Variables

- Primary: Plasma high-density lipoprotein (HDL-cholesterol)
- Secondary: Plasma lipids associated with CVD risk, low-density lipoprotein (LDL), high-density lipoprotein (HDL) and very-low density lipoprotein (VLDL) levels and sub-classes, cholesteryl ester transfer protein (CETP) activity. Incorporation of trans fatty acids to plasma lipids
- Plasma concentrations of HDL-cholesterol, triacylglycerols, total cholesterol, and apoA1 and apoB were measured by enzymatic assays, and LDL-cholesterol was calculated according to the Friedewald method

- Plasma lipoprotein(a) and LDL and HDL particle sizing and distribution profiles were measured by using nuclear magnetic resonance (NMR) spectrometry
- Plasma activity of CETP was measured by fluorimetry
- Fatty acid profiles of plasma cholesteryl esters were analyzed by gas-liquid chromatography
- Fasting body weight and blood pressure were measured at each visit.

Independent Variables

- Diet with trans fatty acids from two different sources
- Profile of fatty acids and trans-fatty acids was carried out using gas chromatography.

Control Variables

- Age
- Weight
- Height
- White and red blood cell counts
- Tryacylglycerols
- Liver parameters (ASAT, ALAT, γ -GT, alkaline phosphatases, bilirubin)
- C-reactive protein
- Glycemia
- Renal parameters (creatinin, urea), sodium and potassium, HIV, HCV serologies and β -HCG (for women)
- Dietary history collected by a dietitian.

Description of Actual Data Sample:

- *Initial N*: 46 (22 men, 24 women)
- *Attrition (final N)*: 40 (21 women, 19 men)
- *Age*: 27.6 ± 7.1 years
- *Ethnicity*: None described
- *Other relevant demographics*: French healthy adults
- *Anthropometrics*: No differences in these:
 - Weight (kg) 64.3 ± 11.0
 - BMI (kg/m^2) 22.0 ± 2.4
 - Waist measurement (cm) 74.3 ± 7.4
- *Location*: France.

Summary of Results:

Modified Table

Serum lipid, lipoprotein and apolipoprotein concentrations; diagnostic ratios in men and women at baseline and after receiving trans-fatty acids (TFA) from natural (rTFA) or industrially produced

sources (iTFA) for three weeks¹

Experimental Periods					
Variable and Subjects	Baseline Values	TFAs from Industrially Produced Sources	TFAs From Natural Sources	Estimated Mean Effect ²	P
HDL-cholesterol (mg/dL)³					
Men	61.7±12.5	58.8±14.8	58.2±14.9	-0.56	0.743
Women	79.6±13.8	73.6±11.9	77.8±13.2	-4.02	0.012
Overall	71.1±15.9	66.6±15.1	68.5±17.0	-2.29	0.037
LDL-cholesterol (mg/dL)³					
Men	91.8±25.9	87.0±27.4	88.7±31.7	-0.03	0.994
Women	99.6±29.2	89.6±25.6	103.1±30.2	-13.75	0.001
Overall	95.9±27.6	88.3±26.6	96.3±31.4	-6.89	0.015
Total cholesterol (mg/dL)³					
Men	169.1±29.1	161.1±31.4	164.0±30.6	-2.02	0.642
Women	195.6±33.1	179.6±30.5	199.5±33.6	-19.98	-0.001
Overall	183.0±33.7	170.8±31.9	182.7±36.5	-11.00	-0.001
Triacylglycerol (log) (mg/dL)					
Men	77.7±25.7	76.3±26.2	85.6±44.2	-0.095	0.994
Women	82.0±30.1	82.1±31.6	93.0±30.3	-0.145	0.001
Overall	80.0±27.8	79.4±28.9	89.5±37.3	-0.055	0.002
ApoA1 (mg/dL)³					
Men	1.32±0.17	1.31±0.21	1.30±0.23	0.00	0.943
Women	1.71±0.28	1.60±0.26	1.72±0.32	-0.12	-0.001
Overall	1.53±0.30	1.46±0.28	1.52±0.35	-0.16	0.012
ApoB (mg/dL)³					
Men	0.71±0.15	0.70±0.16	0.72±0.16	-0.01	0.778
Women	0.81±0.18	0.77±0.18	0.86±0.20	-0.09	-0.001
Overall	0.76±0.17	0.74±0.17	0.79±0.19	-0.05	-0.005
Total:HDL cholesterol					
Men	2.8±0.6	2.9±0.7	2.8±0.6	-0.05	0.616
Women	2.5±0.5	2.6±0.6	2.5±0.5	-0.14	0.128
Overall	2.7±0.6	2.8±0.7	2.6±0.6	-0.09	0.162
ApoA1:apoB					
Men	0.54±0.11	0.56±0.13	0.54±0.13	-0.014	0.644

Women	0.48±0.11	0.51±0.13	0.49±0.12	-0.021	0.165
Overall	0.51±0.11	0.54±0.13	0.52±0.12	-0.008	0.201

¹ N=19 men, 21 women. Apo, apolipoprotein; Lp(a), lipoprotein (a). Results are presented on the per-protocol data set. All plasma variables were analyzed by using a mixed model in week three of treatment, with treatment as the fixed effect, subject as the random effect and sex as the covariate. P<0.05 was considered to be significant.

² Estimate is defined as the difference in clinical outcomes between TFAs from industrially produced and natural sources

³ Treatment x sex interaction was significant (P<0.05)

⁴ Mean ± SD (all such values)

⁵ Evaluated in log-transformed data.

Other Findings

There was no differences in carbohydrate, protein, fat, alcohol and overall energy intake between groups.

Author Conclusion:

- Trans-fatty acids from industrially produced and from natural sources have different effects on CVD risk factors in women
- The HDL-cholesterol-lowering property of TFAs seems to be specific to industrial sources. However, it is difficult in the present study to draw a conclusion about the effect of TFAs from either source on absolute CVD risk in these normolipidemic subjects
- The mechanism underlying the observed sex- and isomer-specific effects warrants further investigation.

Reviewer Comments:

This study was well-designed but for a few omissions by the authors:

- *Authors presented baseline data (see table), but did not indicate how it was used in the analysis and overall interpretation of the results*
- *Authors reported that this was a RCC, double-blind trial. There was not description in the methodology about what procedures were followed to blind either subjects and researchers from intervening diets*
- *No intent to treat in the statistical analysis was described.*

Research Design and Implementation Criteria Checklist: Primary Research

Relevance Questions

1.	Would implementing the studied intervention or procedure (if found successful) result in improved outcomes for the patients/clients/population group? (Not Applicable for some epidemiological studies)	No
2.	Did the authors study an outcome (dependent variable) or topic that the patients/clients/population group would care about?	Yes
3.	Is the focus of the intervention or procedure (independent variable) or topic of study a common issue of concern to nutrition or dietetics practice?	Yes
4.	Is the intervention or procedure feasible? (NA for some epidemiological studies)	No

Validity Questions

1.	Was the research question clearly stated?	Yes
1.1.	Was (were) the specific intervention(s) or procedure(s) [independent variable(s)] identified?	Yes
1.2.	Was (were) the outcome(s) [dependent variable(s)] clearly indicated?	Yes
1.3.	Were the target population and setting specified?	Yes
2.	Was the selection of study subjects/patients free from bias?	Yes
2.1.	Were inclusion/exclusion criteria specified (e.g., risk, point in disease progression, diagnostic or prognosis criteria), and with sufficient detail and without omitting criteria critical to the study?	Yes
2.2.	Were criteria applied equally to all study groups?	Yes
2.3.	Were health, demographics, and other characteristics of subjects described?	Yes
2.4.	Were the subjects/patients a representative sample of the relevant population?	No
3.	Were study groups comparable?	Yes
3.1.	Was the method of assigning subjects/patients to groups described and unbiased? (Method of randomization identified if RCT)	Yes
3.2.	Were distribution of disease status, prognostic factors, and other factors (e.g., demographics) similar across study groups at baseline?	Yes
3.3.	Were concurrent controls used? (Concurrent preferred over historical controls.)	Yes
3.4.	If cohort study or cross-sectional study, were groups comparable on important confounding factors and/or were preexisting differences accounted for by using appropriate adjustments in statistical analysis?	N/A

3.5.	If case control or cross-sectional study, were potential confounding factors comparable for cases and controls? (If case series or trial with subjects serving as own control, this criterion is not applicable. Criterion may not be applicable in some cross-sectional studies.)	N/A
3.6.	If diagnostic test, was there an independent blind comparison with an appropriate reference standard (e.g., "gold standard")?	N/A
4.	Was method of handling withdrawals described?	Yes
4.1.	Were follow-up methods described and the same for all groups?	Yes
4.2.	Was the number, characteristics of withdrawals (i.e., dropouts, lost to follow up, attrition rate) and/or response rate (cross-sectional studies) described for each group? (Follow up goal for a strong study is 80%.)	Yes
4.3.	Were all enrolled subjects/patients (in the original sample) accounted for?	Yes
4.4.	Were reasons for withdrawals similar across groups?	Yes
4.5.	If diagnostic test, was decision to perform reference test not dependent on results of test under study?	N/A
5.	Was blinding used to prevent introduction of bias?	???
5.1.	In intervention study, were subjects, clinicians/practitioners, and investigators blinded to treatment group, as appropriate?	???
5.2.	Were data collectors blinded for outcomes assessment? (If outcome is measured using an objective test, such as a lab value, this criterion is assumed to be met.)	???
5.3.	In cohort study or cross-sectional study, were measurements of outcomes and risk factors blinded?	N/A
5.4.	In case control study, was case definition explicit and case ascertainment not influenced by exposure status?	N/A
5.5.	In diagnostic study, were test results blinded to patient history and other test results?	N/A
6.	Were intervention/therapeutic regimens/exposure factor or procedure and any comparison(s) described in detail? Were intervening factors described?	Yes
6.1.	In RCT or other intervention trial, were protocols described for all regimens studied?	Yes
6.2.	In observational study, were interventions, study settings, and clinicians/provider described?	N/A
6.3.	Was the intensity and duration of the intervention or exposure factor sufficient to produce a meaningful effect?	Yes
6.4.	Was the amount of exposure and, if relevant, subject/patient compliance measured?	Yes

6.5.	Were co-interventions (e.g., ancillary treatments, other therapies) described?	Yes
6.6.	Were extra or unplanned treatments described?	N/A
6.7.	Was the information for 6.4, 6.5, and 6.6 assessed the same way for all groups?	Yes
6.8.	In diagnostic study, were details of test administration and replication sufficient?	N/A
7.	Were outcomes clearly defined and the measurements valid and reliable?	Yes
7.1.	Were primary and secondary endpoints described and relevant to the question?	Yes
7.2.	Were nutrition measures appropriate to question and outcomes of concern?	Yes
7.3.	Was the period of follow-up long enough for important outcome(s) to occur?	Yes
7.4.	Were the observations and measurements based on standard, valid, and reliable data collection instruments/tests/procedures?	Yes
7.5.	Was the measurement of effect at an appropriate level of precision?	Yes
7.6.	Were other factors accounted for (measured) that could affect outcomes?	???
7.7.	Were the measurements conducted consistently across groups?	Yes
8.	Was the statistical analysis appropriate for the study design and type of outcome indicators?	Yes
8.1.	Were statistical analyses adequately described and the results reported appropriately?	Yes
8.2.	Were correct statistical tests used and assumptions of test not violated?	Yes
8.3.	Were statistics reported with levels of significance and/or confidence intervals?	Yes
8.4.	Was "intent to treat" analysis of outcomes done (and as appropriate, was there an analysis of outcomes for those maximally exposed or a dose-response analysis)?	No
8.5.	Were adequate adjustments made for effects of confounding factors that might have affected the outcomes (e.g., multivariate analyses)?	N/A
8.6.	Was clinical significance as well as statistical significance reported?	Yes
8.7.	If negative findings, was a power calculation reported to address type 2 error?	???
9.	Are conclusions supported by results with biases and limitations taken into consideration?	Yes
9.1.	Is there a discussion of findings?	Yes

9.2.	Are biases and study limitations identified and discussed?	Yes
10.	Is bias due to study's funding or sponsorship unlikely?	Yes
10.1.	Were sources of funding and investigators' affiliations described?	Yes
10.2.	Was the study free from apparent conflict of interest?	Yes